UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/173,531	10/15/1998	Ralph M. Ellison	7409-150-999	1947

7590 11/27/2001

STEPHEN A. BENT
FOLEY & LARDNER
3000 K STREET, N.W., SUITE 500
WASHINGTON HARBOUR
WASHINGTON, DC 20007-5109

EXAMINER	
PAK, JOHN D	
ART UNIT	PAPER NUMBER
1616	

DATE MAILED: 11/27/2001

13

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/173,531	Applicant(s) ELLISON et al.
	Examiner Pak, J.	Art Unit 1616

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Aug 21, 2001* .

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-18 and 21-29* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-18 and 21-29* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 12

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

Claims 1-18 and 21-29 are pending in this application.

Applicant's IDS of 8/21/01, filed **after** a first Office action on the merits, cites numerous references that are not in English. References designated by applicant as AT, AU, AW, AX, AY, BB, BL, BR, CG, CP, CS, CU, CW, CX, CZ are not in the English language, applicant has not provided a concise explanation of their relevance according to 37 CFR 1.98(a)(3), and the Examiner is unable to readily understand the reference disclosures. Said references are therefore crossed out in the IDS. It is also noted that references BY and CY are the same; the second citation, i.e. CY, is therefore crossed out.

Claims 16 and 27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(1) There is a minor mistake in claim 16 – at line 4, the comma between "retinoic" and "acid" should be deleted so that it reads "retinoic acid".

(2) Claim 27 refers to the arsenic compound as a "prodrug," i.e. a substance that is itself not active but produces an active metabolite. This is confusing because claims 1, 2 and 3, from which claim 27 depends, read on using arsenic compounds as the active therapeutic agent. Applicant cannot have it both ways: arsenic is either a drug or a prodrug.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 13, 14, 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Stephens et al. (Ref. CN).

Stephens et al. explicitly disclose treating CML patients with a solution of potassium arsenite or solution of potassium arsenite combined with radiation therapy ("roentgen treatments"). See p. 1488, second paragraph; see *for example*, Case 4 on pp. 1492-94. Instant claims, which read on treating any neoplastic disease with arsenic and a "radiotherapeutic agent," are thereby anticipated.

Claims 1-6, 10-11, 13-15, 17 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over CN 1079391 (Ref. AR).

CN 1079391 explicitly discloses various cancer treatments with arsenic compounds. Applicant has provided a translation of this patent document and pages from the translation are referenced herein. CN 1079391 discloses that it is known to treat skin cancer with arsenic, e.g. arsenic trioxide (paragraph bridging pages 6-7). CN 1079391 also discloses that it is known to

treat cervical cancer with arsenic containing formulations (*id.*). CN 1079391 teaches formulating trivalent arsenic oxides, salts, organic compounds or their "compound recipe traditional Chinese medicines" as ointment and paste used for body surfaces and suspended injection and liposome used "for direct injection against in vivo cancer entities" (paragraph bridging pages 7-8). Instant claims are thereby anticipated, or at the very least rendered obvious within the meaning of section 103(a).

Claims 1-2, 4-5, 8, 13-15 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Li et al. (Ref. BY).

Li et al. explicitly disclose treating patients with malignant lymphomas, e.g. Hodgkin's disease) with Ailin injection plus Chinese herbal medicine. See the partial English translation on page 62. Instant claims are thereby anticipated, or at the very least rendered obvious within the meaning of section 103(a), because "Ailin" is known to contain arsenic.

Claims 1-18 and 21-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combined teachings of CN 1121807, CN 1079391, Li et al., Stephens et al. and Shimotsuura et al. in view of Shen et al., Konig et al. and JP 51-88620.

Applicant's claims read on treating practically every known cancer with arsenic compounds. Arsenic has a long history of use as an anticancer agent and recently there has been a

resurgence of interest; accordingly, the breadth of claims and extensiveness of the prior art necessitate the many references relied upon in this ground of rejection.

CN 1121807 (Ref. AQ) teaches treating acute leukemia, liver cancer and lymphatic cancer with a solution formulated with 1-10 g arsenic trioxide, 8 g sodium chloride, 1000 ml water (see translation p. 4, last paragraph, translation p. 5, first paragraph). The formulation exhibits a variety of activity, including inhibition of DNA and RNA synthesis, loss of ability of clone proliferation, killing effect of leukemia cells, restoration of bone marrow hemopoietic functions (translation p. 5, second paragraph). 10 ml injection per day is disclosed for adults, with different dosage and concentrations being possible based on age and condition (translation p. 5, last full paragraph).

CN 1079391(Ref. AR) discloses various cancer treatments with arsenic compounds. CN 1079391 discloses that it is known to treat skin cancer with arsenic, e.g. arsenic trioxide (paragraph bridging translation pp. 6-7). CN 1079391 also discloses that it is known to treat cervical cancer with arsenic containing formulations (*id.*). CN 1079391 teaches formulating trivalent arsenic oxides, salts, organic compounds or their "compound recipe traditional Chinese medicines" as ointment and paste used for body surfaces and suspended injection and liposome used "for direct injection against in vivo cancer entities" (paragraph bridging translation pp. 7-8).

Li et al. (Ref. BY) disclose treating patients with malignant lymphomas, e.g. Hodgkin's disease) with Ailin injection plus Chinese herbal medicine. See the partial English translation on page 62.

Stephens et al. disclose treating CML patients with a solution of potassium arsenite or solution of potassium arsenite combined with radiation therapy ("roentgen treatments"). See p. 1488, second paragraph; see *for example*, Case 4 on pp. 1492-94.

Shimotsuura et al. (cited in previous Office action) disclose the antineoplastic action of arsenic trioxide . See the entire article, in particular the Conclusion section in p. 49 of the original article. See also pages 52-53 of an English summary, as well as the provided English translation.

Shen et al. (cited in previous Office Action) disclose treating APL with arsenic trioxide. 10 mg arsenic trioxide was administered via IV drip (see the entire article).

Konig et al. (Ref. BV) disclose that the organic arsenic compound melarsoprol has similar antineoplastic activity as arsenic trioxide and induces apoptosis (pp. 567-69).

JP 51-88620 (Ref. AI) disclose that a mixture of ferrous, arsenic and sulfate ions can "cure cancerous disease of stomach, duodenum, uterus, lung, pancreas, etc." (see the entire document and the provided English abstract).

While the cited references do not explicitly disclose the treatment of every single different type of cancers recited in applicant's claims with arsenic compounds, it is clear from the combined teachings of the prior art that arsenic compound containing compositions can be expected to have therapeutic effect against variety of cancer types, including acute leukemia, liver cancer, lymphatic cancer (CN 1121807), skin cancer, cervical cancer, cancer of body surfaces and "in vivo cancer entities" (CN 1079391), malignant lymphomas such as Hodgkin's disease (Li et al.), CML (Stephens et al.), APL (Shen et al.), and various cancers of major organs (JP 51-88620), taken

with additional supportive in vitro antineoplastic data (Shimotsuura et al. and Konig et al.). Given the different types of cancers that arsenic containing formulations have been taught to be useful in the prior art, in light of the recent clinical success (e.g. Shen et al.) in treating APL with arsenic trioxide, one having ordinary skill in the art would have expected broad anticancer activity and would have been motivated to utilize arsenic containing compositions for treating the various cancer types now recited in applicant's claims. Use with other chemotherapeutic agents or radiotherapeutic agents, various administration techniques and forms, and various specific arsenic compounds would have been well suggested from the known combined use of many different treatments to fight cancer, the known conventional chemotherapy techniques and formulation/delivery methods, and the known or expected anticancer activity of various arsenic compounds (arsenic trioxide, Fowler's solution, arsenic ions, melarsoprol, etc.), respectively.

Therefore, the claimed invention, as a whole, would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, because every element of the invention has been fairly suggested by the teachings of the cited reference.

Applicant's arguments filed in Paper No. 11 (8/21/01), including the Chen declaration, are not directly relevant to the new ground of rejection herein, which applies new references submitted by applicant after the first Office action on the merits. With regard to statements supposedly made by the Examiner in another application, applicant is advised that the Examiner cannot comment on the prosecution of another unrelated application. In any event, applicant is reminded that enablement is a factual issue, which depends on, inter alia, the filing date in

question, state of the art at the time of the invention, etc. Here, the filing date of this application is 10/15/98, with a domestic claim of priority of 10/10/15/97, which must be many years later than the effective filing date of the other application to which applicant refers. Information developed after the effective filing date of another earlier application but before the effective filing date of the instant applicant may necessitate a different conclusion under the facts of this application.

For these reasons, no claim can be allowed at this time.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

A facsimile center has been established in Technology Center 1600. The hours of operation are Monday through Friday, 8:45 AM to 4:45 PM. The telecopier numbers for accessing the facsimile machines are (703) 308-4556 or (703) 305-3592.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Examiner Pak whose telephone number is (703) 308-4538. The Examiner

can normally be reached on Monday through Thursday from 8:00 AM to 5:30 PM. The Examiner can also be reached on alternate Fridays.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's Supervisor, Mr. José Dees, can be reached on (703) 308-4628.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-1235.

JOHN PAK
PRIMARY EXAMINER
GROUP 1600